

We claim:

1. A DNA sequence encoding at least a portion of at least one β -chain antigen of the HLA-DR locus of the human lymphocyte antigen complex, said sequence being selected from the group consisting of

(a) the DNA inserts DR- β -A, DR- β -B and DR- β -C,

(b) DNA sequences which hybridize under high criterium thereto, and

(c) DNA sequences which when expressed code for the polypeptides coded for by the expression of any of the foregoing DNA sequences or inserts,

said sequences and inserts encoding a product that displays an immunological or biological activity of a β -chain of the HLA-DR locus.

2. The DNA sequence of claim 1, wherein said sequence (b) which hybridizes to said sequence (a) is selected from the group consisting of:

(d) the DNA insert of DR- β -D,

(e) DNA sequences which hybridize under high criterium thereto;

(f) DNA sequences which when expressed code for the polypeptides coded for by the expression of any of the foregoing DNA sequences or inserts,

said sequences and inserts encoding a product that displays an immunological or biological activity of a β -chain of the HLA-DR locus.

3. A DNA sequence selected from the group consisting of:

ATGGTGTGTCTGAAGCTCCCTGGAGGCTCCAGCTTGGCAGCGTTGACAGTG
ACACTGATGGTGCTGAGCTCCCGACTGGCTTTCGCTGGGGACACCCGACCA
CGTTTCTTGGAGCTGCTTAAGTCTGAGTGTCATTTCTTCAATGGGACGGAG

CGGGTGCGGTTCTTGGAGAGACACTTCCATAACCAGGAGGAGTACGCGCGCT
 TCGACAGCGACGTGGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTGA
 TGCCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGGGGCCAG
 GTGGACAATTACTGCAGACACAACACTACGGGGTGTGGAGAGCTTCACAGTGC
 5 AGCGGCGAGTCCATCCTCAGGTGACTGTGTATCCTGCAAAGACCCAGCCCCT
 GCAGCACCACAACCTCCTGGTCTGCTCTGTGAGTGGTTTCTATCCAGGCAGC
 ATTGAAGTCAGGTGGTTCCGGAACGGCCAGGAAGAGAAGGCTGGGGTGGTGT
 CCACGGGCCTGATCCAGAATGGAGACTGGACCTTCAGACCCTGGTGATGCT
 AGAAACATTTCTCCTCGGAGTGGAGAGGTTTACACCTGCCAAGTGGAGCACCCA
 10 AGCGTAACGAGCCCTCTCACAGTGAATGGAGTGCACGGTCTGAATCTGCAC
 AGAGCAAGATGCTGAGTGGAGTCGGGGGCTTTGTGCTGGGCCTGCTCTTCCT
 TGGGGCCGGGCTGTTTCTACTTTCAGGAATCAGAAAGGACACTCTGGACTT
 CAGCCAACAGGATTCCTGAGC and GGGGACACCCGACCACGTTTCTTG
 GAGCTGCTTAAGTCTGAGTGTCAATTTCTTCAATGGGACGGAGCGGGTGC
 15 TCCTGGAGAGACACTTCCATAACCAGGAGGAGTACGCGCGCTTCGACAGCGA
 CGTGGGGGAGTACCGGGCGGTGAGGGAGCTGGGGCGGCCTGATGCCGAGTAC
 TGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGGGGCCAGGTGGACAATT
 ACTGCAGACACAACACTACGGGGTGTGGAGAGCTTCACAGTGCAGCGGCGAGT
 CCATCCTCAGGTGACTGTGTATCCTGCAAAGACCCAGCCCCTGCAGCACCAC
 20 AACCTCCTGGTCTGCTCTGTGAGTGGTTTCTATCCAGGCAGCATTGAAGTCA
 GGTGGTTCCGGAACGGCCAGGAAGAGAAGGCTGGGGTGGTGTCCACGGGCCT
 GATCCAGAATGGAGACTGGACCTTCAGACCCTGGTGATGCTAGAAACATTT
 CCTCGGAGTGGAGAGGTTTACACCTGCCAAGTGGAGCACCCAAGCGTAACGA
 GCCCTCTCACAGTGAATGGAGTGCACGGTCTGAATCTGCACAGAGCAAGAT
 25 GCTGAGTGGAGTCGGGGGCTTTGTGCTGGGCCTGCTCTTCCTTGGGGCCGGG
 CTGTTTCTACTTTCAGGAATCAGAAAGGACACTCTGGACTTCAGCCAACAG
 GATTCCTGAGC.

4. A DNA sequence selected from the group
 consisting of: TGGAGTCTTAAGTCTGA, TCCTGGAGAGACAC
 30 TTCCA, GGGGCCAGGTGGACAATTA, and GCTTCGACAGCGACGTGGG.

5. A DNA sequence selected from the group
 consisting of:

ATGGTGTGTCTGAAGTTCCCTGGAGGCTCCTGCATGGCAGCTCTGACAGTG
 ACACTGATGGTGTGCTGAGCTCCCCACTGGCTTTGGCTGGGGACACCCGACCA
 35 CGTTTCTTGGAGCAGGTTAAACATGAGTGTCAATTTCTTCAACGGGACGGAG
 CGGGTGCGGTTCTTGGACAGATACTTCTATCACCAAGAGGAGTACGTGCGC

TTCGACAGCGACGTGGGGGAGTACCGGGGGGTGACGGAGCTGGGGCGGCCT
 GATGCCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGGGCC
 GCGGTGGACACCTACTGCAGACACAACCTACGGGGTTGGTGAGAGCTTCACA
 GTGCAGCGGCGAGTCTATCCTGAGGTGACTGTGTATCCTGCAAAGACCCAG
 5 CCCCTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGTTTCTATCCA
 GGCAGCATTGAAGTCAGGTGGTTCCGGAACGGCCAGGAAGAGAAGACTGGG
 GTGGTGTCCACAGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACCCTG
 GTGATGCTGGAAACAGTTCCTCGGAGTGGAGAGGTTTACACCTGCCAAGTG
 GAGCACCCAAGCCTGACGAGCCCTCTCACAGTGGAATGGAGAGCACGGTCT
 10 GAATCTGCACAGAGCAAGATGCTGAGTGGAGTCCGGGGCTTCGTGCTGGGC
 CTGCTCTTCCTTGGGGCCGGGCTGTTTCATCTACTTCAGGAATCAGAAAGGA
 CACTCTGGACTTCAGCCAACAGGATTCTGAGC and GGGGACACCCGA
 CCACGTTTCTTGGAGCAGGTTAAACATGAGTGTCAATTTCTTCAACGGGACG
 GAGCGGGTGCGGTTCTGACAGATACTTCTATCACCAAGAGGAGTACGTG
 15 CGCTTCGACAGCGACGTGGGGGAGTACCGGGCGGTGACGGAGCTGGGGCGG
 CCTGATGCCGAGTACTGGAACAGCCAGAAGGACCTCCTGGAGCAGAAGCGG
 GCCGCGGTGGACACCTACTGCAGACACAACCTACGGGGTTGGTGAGAGCTTC
 ACAGTGCAGCGGCGAGTCTATCCTGAGGTGACTGTGTATCCTGCAAAGACC
 CAGCCCCTGCAGCACCACAACCTCCTGGTCTGCTCTGTGAATGGTTTCTAT
 20 CCAGGCAGCATTGAAGTCAGGTGGTTCCGGAACGGCCAGGAAGAGAAGACT
 GGGGTGGTGTCCACAGGCCTGATCCAGAATGGAGACTGGACCTTCCAGACC
 CTGGTGATGCTGGAAACAGTTCCTCGGAGTGGAGAGGTTTACACCTGCCAA
 GTGGAGCACCCAAGCCTGACGAGCCCTCTCACAGTGGAATGGAGAGCACGG
 TCTGAATCTGCACAGAGCAAGATGCTGAGTGGAGTCCGGGGCTTCGTGCTG
 25 GGCCTGCTCTTCCTTGGGGCCGGGCTGTTTCATCTACTTCAGGAATCAGAAA
 GGACACTCTGGACTTCAGCCAACAGGATTCTGAGC.

6. A DNA sequence selected from the group consisting of TGGAGCAGGTTAAACATGA, TCCTGGACAGATACTTCTA, and GGGCCGCGGTGGACACCTA.

7. A DNA sequence selected from the group consisting of DNA insert DR- β -C, the expressed portion of the DNA insert of DR- β -C, and fragments of either member of this group that encode products displaying an immunological or biological activity of a β -chain of the HLA-DR locus.

8. A DNA sequence selected from the group consisting of DNA insert DR- β -D, the expressed por-

tion of the DNA insert of DR- β -D, and fragments of either member of this group that encode products displaying an immunological or biological activity of a β -chain of the HLA-DR locus.

5 9. A recombinant DNA molecule comprising a DNA sequence selected from the DNA sequences of any one of claims 1-3, 5 and 7-8.

10 10. The recombinant DNA molecule of claim 9 wherein the DNA sequence is operatively linked to an expression control sequence in said recombinant DNA molecule.

15 11. A polypeptide displaying an immunological or biological activity of at least one β -chain antigen of the HLA-DR locus of the human lymphocyte antigen complex produced by a process of culturing a host transformed with the recombinant DNA molecule of claim 10.

20 12. A polypeptide selected from the group consisting of polypeptides of the formula:
MVCLKLPGGSSLAALTVTLMVLSSRLAFAGDTRPRFLELLKSECHFFNGTE
RVRFLERHFFHNQEEYARFDSVGEYRAVRELGRPDAEYWNSQKDLLEQKRG
QVDNYCRHNYGVVESFTVQRRVHPQVTVYPAKTQPLQHNNLLVCSVSGFYF
GSIEVRWFRNGQEEKAGVVSTGLIQNGDWTFTQTLVMLETTFPRSGEVYTCQV
EHPSVTSPPLTVEWSARSESAQSKMLSGVGGFVLGLLFLGAGLFIYFRNQKG
25 HSGLOPTGFLS and GDTRPRFLELLKSECHFFNGTERVRFLEHFFHNQEEYARFDSVGEYRAVRELGRPDAEYWNSQKDLLEQKRGQVDNYCRHNYGVV
ESFTVQRRVHPQVTVYPAKTQPLQHNNLLVCSVSGFYFPGSIEVRWFRNGQEEKAGVVSTGLIQNGDWTFTQTLVMLETTFPRSGEVYTCQVEHPSVTSPPLTVEW
SARSESAQSKMLSGVGGFVLGLLFLGAGLFIYFRNQKGHSGLOPTGFLS.

30 13. A polypeptide selected from the group consisting of polypeptides of the formula:

35 MVCLKFPGGSCMAALTVTLMVLSSPLALAGDTRPRFLEQVKHECHFFNGTE
RVRFLDRYFYHQEEYVRFDSDVGEYRAVTELGRPDAEYWNSQKDLLEQKRA
AVDTYCRHNYGVGESFTVQRRVYPEVTVYPAKTQPLQHNNLLVCSVNGFYF
GSIEVRWFRNGQEEKTGVVSTGLIQNGDWTFTQTLVMLETTFPRSGEVYTCQV
EHPSLTSPPLTVEWRARSESAQSKMLSGVGGFVLGLLFLGAGLFIYFRNQKG
HSGLOPTGFLS and GDTRPRFLEQVKHECHFFNGTERVRFLEDRYFYHQE

EYVRFDSVDGEYRAVTELGRPDAEYWN\$QKDLLEQKRAAVDTYCRHNYGVG
ESFTVQRRVYPEVTVYPAKTQPLQHNNLLVCSVNGFYPGSIEVRWFRNGQE
EKTGVVSTGLIQNGDWFQTLVMLETVPRSGEVYTCQVEHPSLTSPLTVEW
RARSESAQSKMLSGVGGFVLGLLFLGAGLFIYFRNQKGHSGLOPTGFLS.

5 14. A process for producing a DNA sequence
encoding at least one β -chain antigen of the HLA-DR
locus of the human lymphocyte antigen complex com-
prising the steps of culturing a host transformed
with a recombinant DNA molecule of claim 9, and iso-
10 lating said DNA sequence.

15 15. A process for producing a polypeptide
displaying an immunological or biological activity
of at least one β -chain antigen of the HLA-DR locus
of the human lymphocyte antigen complex comprising
the steps of culturing a host transformed with a
recombinant DNA molecule of claim 10 and collecting
the polypeptide.

20 16. An HLA-DR typing process comprising
the steps of restricting DNA isolated from the
individual to be typed with at least one restriction
endonuclease; size fractionating the restricted DNA;
hybridizing the size-fractionated DNA to a DNA
sequence of any one of claims 1 to 8 and detecting
the areas of hybridization.

25 17. The process of claim 16, wherein a
³²P-labelled DNA sequence is employed for hybridiza-
tion and its radioactive label is used for detecting
the areas of hybridization.

30 18. An HLA-DR typing process comprising
the steps of restricting DNA isolated from the
individual to be typed with at least one restriction
endonuclease; size fractionating the restricted DNA;
hybridizing the sizefractionated DNA to a 19-mer
selected from the group consisting of TGGAGCTGCTTAAG
35 TCTGA, TCCTGGAGAGACACTTCCA, GGGGCCAGGTGGACAATTA,
TGGAGCAGGTAAACATGA, TCCTGGACAGATACTTCTA, and GGGCCG
CGGTGGACACCTA.

19. The typing process of claim 18 wherein the hybridization control is a 19-mer of the formula GCTTCGACAGCGACGTGGG.

5 ^{sub A2} 20. An HLA-DR typing kit characterized by a DNA sequence of any one of claims 1 to 8.

21. In an HLA-DR typing process, the improvement comprising employing a polypeptide of claim 11-13 or an antibody raised against those polypeptides.

10 22. In an HLA-DR typing kit, the improvement comprising employing a polypeptide of claim 11-13 or an antibody raised against those polypeptides.

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a₃

add
B10

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D2

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E1

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C5

add
F1